Alzheimer's & Dementia: The Journal of the Alzheimer's Association

Brain health: key to health, productivity, and wellbeing

--Manuscript Draft--

Manuscript Number:	
Article Type:	Perspective
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Cover Letter

11 July 2021

Zaven S. Khachaturian, PhD
Editor-in-Chief
Alzheimer's & Dementia

Dear Dr Khachaturian,

Please consider our Perspective manuscript entitled “Brain health: key to health, productivity, and wellbeing” for publication in *Alzheimer's & Dementia*. It reviews current efforts and convergent paths, rationale for joint collaborations, threatening and encouraging trends, challenges in promoting and maintaining brain health, and available definitions of brain health. We also propose next steps in fostering brain health. This paper will provide a platform for debate on the importance of fostering brain health, for making it the top global priority, and for providing an opportunity to challenge current thinking. It could also shed light on the interconnectedness of physical, mental, environmental, and socioeconomic determinants of brain disease and health. The manuscript and figures are prepared according to the journal standards and every section is within the limits. It involves 42 co-authors from five continents to make the mission and vision inclusive and worldwide.

If we may, we would suggest the following potential reviewers for our manuscript.

- Claudia Kawas (University of California, Irvine, CA) <ckawas@hs.uci.edu>;
- Gunnar Bovim (Norwegian University of Science and Technology, Trondheim, Norway) <gunnar.bovim@ntnu.no>;
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Looking forward to a prompt and positive review.
Best regards,
Abolfazl Avan and Vladimir Hachinski

Brain health: key to health, productivity, and wellbeing

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Word counts: Title 56 characters; Abstract 150 words; Body text 4815 words (including 3 Boxes with 1354 words); 3 Figures (legends 356 words), and 50 References (1260 words).

Keywords: Brain health; mental health; collaboration; stroke; dementia; ischemic heart disease; triple threat; definition; prevention; promotion; Brain Health Learn and Act Group;

Abstract

Brain health is essential for physical and mental health, social wellbeing, productivity, and creativity. Current neurological research focuses mainly on treating a diseased brain and preventing further deterioration rather than on developing and maintaining brain health. The pandemic has forced a shift towards virtual working environments that accelerated opportunities for transdisciplinary collaboration for fostering brain health among neurologists, psychiatrists, psychologists, neuro and socio-behavioral scientists, scholars in arts and humanities, policymakers, and citizens. This could shed light on the interconnectedness of physical, mental, environmental, and socioeconomic determinants of brain disease and health. We advocate making brain health the top priority worldwide, developing common measures and definitions to enhance research and policy, and finding the cause of the decline of incidence of stroke and dementia in some countries. Then apply comprehensive customized cost-effective prevention solutions in actionable implementation units. Life cycle brain health offers the best single individual, communal, and global investment.

Research In Context

Systematic review: We reviewed literature using PubMed and websites using Google for terms related to brain health. We aimed to summarize current efforts, plans, and challenges in promoting brain health.

Interpretation: Current efforts mainly focus on detecting and treating diseased brains, rather than improving or maintaining brain health. There are disparities in health care access, inequities, discriminations, and lack of funds for studies in this field. The most promising strategy is a lifetime holistic approach to prevention of brain diseases and to promotion of brain health.

Future directions: Brain health should become the top priority worldwide. We should gather and converge transdisciplinary expertise on brain health. We need to develop global workgroups and workforces aiming to promote healthy aging through the life-course through electronic, social, and print media. Further, we need to establish an ecosystem to engage synergistically the population, patients, health-care providers, payers for health services, and policymakers.

1. Introduction

Progress poses paradoxes: economic growth, prolongation of life expectancy, and increased literacy alongside climate deterioration, growing socioeconomic and health inequalities, and in some circumstances declining happiness and mental health.[1,2] This realization has driven the development of increasingly sophisticated wellbeing metrics. Such measures can be divided into three general categories: 1) Hedonic, reflecting the individual's daily affective state; 2) Evaluative of the person's satisfaction of life over a lifetime; and 3) Eudemonic in having a purpose or meaning in life.[2] Satisfied individuals are more productive and productivity contributes to wellbeing. Good brain health is the common mediator for both, and good brain health is dependent on a healthy body living in nurturing social and natural communities.

Most neurological research focuses on detecting and treating diseased brains, rather than how brain health can be developed, improved, and maintained as we age. Currently, prevention of brain diseases is mostly based on controlling risk factors and to a lesser extent on encouraging protective factors and improving resilience. However, we must also incorporate common physical, psychological, behavioral, environmental (e.g., air pollution, climate change), and socioeconomic measures (e.g., income, social status, and education), as well as age, gender, genetics, and ethnocultural background in our models. The coronavirus disease 2019 (COVID-19) pandemic allowed us to realize the crucial importance of the One Health approach, i.e. the interconnectedness of all life forms (humans, nonhumans, and the earth) as the fundamental determinant of brain health and overall health.[3] The factors that promote brain health are diverse, abundant, and interactive.

According to the World Health Organization (WHO), health is "*a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity*." Given that all our behaviors, actions, and interactions result from the brain's activity, the key to fulfilling the WHO definition depends on brain health. We are our brains, as Hippocrates recognized 2500 years ago: "*From the brain and from the brain only, arise our pleasures, joys, laughter and jests as well as our sorrows, pains, griefs and tears. Through it, we think, see, hear, and distinguish the ugly from the beautiful, the bad from the good*." Transdisciplinary collaboration and systems science approaches are needed to overcome gaps and hurdles in achieving or maintaining comprehensive brain health (Box 1).[4]

As we are learning from the COVID-19 pandemic, one underlying cause can lead to myriads of conditions. This highlights the interconnectedness of human health with all life forms and environments.[3] Although each of the presentations frequently needs to be treated separately, all have one fundamental cause—i.e., COVID-19—that requires prevention or treatment. Like the story of *'The Blind Men and the Elephant'* or *'The Elephant in the Dark'* shown in Figure 1, if we focus only on one aspect of brain health, we will not achieve optimal success. Rumi, the thirteenth century Persian poet, retold the story of an elephant exhibited in a dark room: several men touch and feel the elephant in the dark and, depending upon where they touch it, they draw different conclusions about what it is. He used this story as an example of the limits of individual perception. He stated that if each had a 'candle' and they went in 'together' the differences would disappear. Sometimes the problem is more complex than this

standard scenario as the blind men may actually be in a zoo palpating different animals, not the same elephant. Different underlying diseases may lead to similar consequences, e.g. cognitive decline and dementia resulting from Alzheimer's disease, multiple strokes, uncontrolled seizures, Parkinson's disease, etc.: "*One brain, one person, multiple diseases*."

In this Perspective, we discuss current efforts, plans, gaps, and challenges (Box 1), rationale for joint collaborations, current definitions of brain health (Box 2), and propose next steps (Box 3) in achieving the optimum goal of promoting overarching brain health.

1.1. Aims

- To elaborate on the importance of brain health for overall health, wellbeing, and productivity.
- To make clear that cognitive health is dependent not only on the nervous system but also on body and social health.
- To identify the lack of a uniform definition of brain health endorsed by major societies
- To review historical data on current brain health definitions and to explore whether they are operationalized by providing definition criteria.
- To discuss the challenges of maintaining brain health, including disparities in health care access, inequities, discriminations, and lack of funds for studies in this field.
- To highlight potential in fostering brain health and suggest next steps.

2. Search strategy

Because of the scarcity of evidence, particularly with the limited number of publications on the topic, references were identified by searches of websites, reports from organizations, and government reports using Google and PubMed until 15 April 2021, as well as references from relevant articles. We searched using the terms ‘brain health’, ‘healthy brain’, ‘brain resilience’, ‘cognitive health’, and ‘mental health’. There were no language restrictions.

3. Finding and following convergent paths

In 2018, the United Nations listed mental health conditions (including mental, neurological, and substance use disorders) next to cancers, cardiovascular diseases, diabetes, and chronic respiratory diseases as global and national healthcare priorities. While a step forward, this classification perpetuates an artificial distinction between mental and brain diseases. Most mental disorders are associated with functional and/or structural brain abnormalities. For example, all addictions target the same brain areas, and vascular risk factors contribute to mood disorders.[5]

To attract the attention of worldwide policymakers and to converge multidisciplinary expertise on mental and brain diseases, in 2010, under the presidency of one of us (VH), the World Federation of Neurology (WFN) changed its mission to “*fostering quality neurology and brain health worldwide*” and to advocate for amelioration of five key factors of healthy brain: exercise, sleep, environment, diet, and access to care. In 2011, with the WFN-VH led the formation of the World Brain Alliance in Geneva comprising: the Alzheimer's Disease

International, the WFN, the European Brain Council, the International Brain Research Organization, the International Child Neurology Association, the World Federation of Neurorehabilitation, the World Stroke Organization, the World Federation of Neurosurgical Society, and the World Psychiatry Association.[6] The World Brain Alliance was founded on three premises:[6]

1. "The brain is key to health and wellness,
2. Brain health and health begin with the mother's and the child's and their education,
3. Our brains are our future."

At the 66th (2013) World Health Assembly, the WHO announced a comprehensive mental health action plan for 2013–2017. The 72nd (2019) Assembly reinforced and extended this plan until 2030 by aligning it with goals for sustainable development. The following objectives were outlined:[7]

1. “to strengthen effective leadership and governance for mental health;
2. to provide comprehensive, integrated and responsive mental health and social care services in community-based settings;
3. to implement strategies for promotion and prevention in mental health;
4. to strengthen information systems, evidence and research for mental health.”

The European Brain Council, the European Federation of Neurological Associations (EFNA), and the European Academy of Neurology (EAN) aim to persuade the European community to adopt brain health as the top health priority and encourage the formation of national brain health

plans. In 2017, the Norwegian government launched a *Norwegian National Brain Health Strategy (2018–2024)* that incorporates key objectives of enhancing prevention strategies and improving brain health.[8] Poland might be the second.

In recognition of the global importance of brain health, the OneNeurology partnership and the WHO Brain Health Unit have recently (2021) been launched, and a call for global collaboration for brain health was made.[4] The OneNeurology is a joint initiative of the EFNA and the EAN aiming to unite and strengthen neurology-related groups to stimulate collaborative advocacy, action and accountability for the prevention, treatment, and management of neurological disorders worldwide.

In 2018, the American counterparts, the Alzheimer's Association and the Centers for Disease Control and Prevention (CDC) released their third 'action agenda', *Healthy Brain Initiative State and Local Public Health Partnerships to Address Dementia: The 2018–2023 Road Map*,[9] with twenty-five specific actions in four domains of public health:

1. "Educate and empower;
2. Develop policies and mobilize partnerships;
3. Assure a competent workforce; and
4. Monitor and evaluate."

Their aims are to make progress in risk identification and risk reduction, diagnosis, education, and training, help meet the needs of caregivers, and to promote cognitive health. Earlier, in

2014, the CDC established the Healthy Brain Research Network, a thematic public health research network, that gathers interdisciplinary expertise from six leading academic institutions across the United States of America (USA). In 2010, the American Heart Association/American Stroke Association (AHA/ASA) launched the campaign to promote ideal cardiovascular health (life's simple seven) and recognized the critical links between vascular determinants and brain health.[10,11] In 2021, the AHA/ASA also identified the importance of educating and involving primary care providers in optimizing brain health.[12]

A collaborative network has been formed between the University of California, San Francisco and Trinity College, Dublin to protect against dementia and improve brain health worldwide.[13] They aim to train and connect next generation leaders in brain health, to expand preventions and interventions, and to share knowledge and engage in advocacy.

A parallel international effort updated the World Stroke Organization's proclamation calling for the prevention of stroke and potentially preventable dementia, as stroke doubles the risk of dementia.[14,15] It is endorsed by the WFN, the World Heart Federation, Alzheimer's Disease International, the European Brain Council, the AHA/ASA, the Alzheimer Association, and 16 other international, regional, and national organizations. The scientific bases for the joint prevention of stroke and dementia are laid out in the Berlin Manifesto, *Preventing dementia by preventing stroke*, and in the World Stroke Organization declaration, *Global prevention of stroke and dementia*.[15]

Furthermore, in May 2017, the World Health Assembly endorsed the *Global action plan on the public health response to dementia 2017–2025*,[16] providing a comprehensive action plan for policymakers, international, regional, and national partners, and the WHO across seven areas:[16]

1. "Dementia as a public health priority;
2. Dementia awareness and friendliness;
3. Dementia risk reduction;
4. Dementia diagnosis, treatment, care and support;
5. Support for dementia carers;
6. Information systems for dementia;
7. Dementia research and innovation."

The Group of Seven (G7) aims to align societies and governments among the major market democracies—the USA, Japan, Germany, the United Kingdom (UK), France, Italy, and Canada—plus the European Union (EU). G7 summits have addressed maternal, newborn, and child health since 1996 and made a major contribution at the 2010 Canadian hosted summit. The G7 first addressed brain health in 2016 when it declared: "*We also commit to promoting active ageing, with due consideration to gender specific aspects, through multi-sectoral approaches including the promotion of age-friendly communities and support for communities to become dementia-friendly*."[17] Likewise, the broader, more diverse Group of Twenty (G20) summit first addressed brain health in 2019, when it promised to "*improve quality of lives of people with dementia and caregivers*."[18] It also called for interdisciplinary research efforts and promotion

of sharing knowledge on age-related diseases. G7 members increased their compliance with the key mental health commitments from 25% in 2017 to 75% in 2018, while G20 members complied with their 2019 commitment at 53%.[18–20] This indicates that G7 and even G20 summits may effectively govern the promotion of brain health.

4. Rationale for joint collaborations on brain health

4.1. Threatening trends

The ageing of the world's population fuels an expanding burden on healthcare systems of chronic mental and vascular diseases and multimorbidity. It also increases economic demands on a shrinking labor force. Globally, burden of neurological disorders measured by disability-adjusted life years (DALYs) lost, were estimated at 276 million (11.6% of all causes with 15% increase between 1990–2016),[21] mental disorders at 125 million (4.9% of all causes with 4.8% increase between 1990–2019) and substance use disorders at 35 million (1.4% of all causes with 1.7% decrease, although non-significantly, between 1990–2019) globally.[22] However, it is argued that the burden of mental and substance use disorders actually accounts for 13.0% of DALYs.[23] All these brain disorders combined currently constitute the largest cause of death and disability combined (17.9% of DALYs from all causes).

The combination of stroke (143 million DALYs), ischemic heart disease (182 million DALYs), and dementia (25 million DALYs) account for the largest proportion of the global burden of diseases.[24,25] These three diseases (*The Triple Threat*) share the same risk and protective factors, pose risks for each other, and are preventable to different degrees.[24,25] We tend to

manage one disease at a time, but multimorbidity is much more common than single diseases, especially in the elderly.

The global lifetime risk of stroke is one in four adults from the age of 25 years onwards.[26] With roughly 12 million new stroke events per year created over 100 million stroke patients worldwide in 2017, 77% living in low- and middle-income countries (LMICs).[27] The estimated global treatment, rehabilitation, and indirect costs for stroke are more than US$700 billion annually.

Worldwide, approximately 59 million people have had dementia in 2020; 61% of those afflicted were living in LMICs.[28] The prevalence of dementia is projected to reach 82 million in 2030 and 152 million in 2050, with nearly 10 million new cases each year (one every 3 seconds), 71% occurring in LMICs.[28] This is while most efforts in finding a treatment for Alzheimer's disease and related dementias or cognitive decline have been on decreasing its known neuropathological substrates, or on decreasing its biomarkers. Although a controversial anti-amyloid therapy for mild Alzheimer's disease has only recently been approved in the US, no effective treatment for patients with Alzheimer's disease and related dementias exists.

Poor sleep and insufficient sleep is a risk for stroke and dementia. It affects over 20% of the general population, is associated with reduced performance and wellbeing, and costs over $600 billion of healthcare expenditure a year across five OECD countries (Canada, USA, UK, Germany, Japan). Furthermore, unhealthy sleeping habits have been linked with body, brain, and mental

health problems including cardiovascular and metabolic diseases, impaired immunity, cancer, dementia, stroke, and depression.

4.2. Encouraging trends

At least 94% of ischemic heart disease, 86% of stroke, and 40% of dementia is potentially preventable.[25,29] The age-specific incidence rate per 100,000 population of ischemic heart disease, stroke, and dementia has decreased in high-income countries.[25] Declines in dementia risk have been attributed to increasing levels of education and improved control of modifiable vascular risk factors, such as intensive multidomain lifestyle interventions which improve cognition (The FINGER study), lower blood pressure targets being better for the brain and reducing the risk of mild cognitive impairment,[30] and anticoagulants that decrease the risk of dementia in patients with atrial fibrillation.[31] The success of the original FINGER study in Finland led to the launch of similar multidomain interventions in other countries, such as the USA, the Netherlands, France, Singapore, Australia, and many others listed in the World Wide FINGERS collaborative network.[32] Unfortunately, these same encouraging trends do not hold true for the LMICs where demographic shifts in the population are seeing increases in risk factor prevalence and a reduction in age of the same. In contrast, developing countries are beginning to develop population-based strategies to reduce the rising burden of stroke and cardiovascular disease and underlying risk factors such as hypertension in the first place.[14] The National Academy of Medicine identified blood pressure management, increasing physical activity, and cognitive training as having the most encouraging, although inconclusive, evidence to delay age-related cognitive decline or prevent dementia.[33]

Increasing attention is being paid to protective factors and resilience. In individuals with the same burden of brain pathology, some are demented while others are not. Education and physical and social activity are protective of late age cognitive decline, independent of Alzheimer's pathology. Improving purpose in life may increase healthspan and add dementia-free years.[34] Considering the bidirectional relationship between sleep and stroke, and sleep and dementia, improving sleep may improve brain health.[35] Likewise, for bidirectional relationship between depression and cerebrovascular diseases or depression and dementia.[5,36]

The pandemic crisis appears to have propelled social justice-based movements against systemic discrimination, racism, and inequality, all of which have been linked to a range of adverse health outcomes. Brain health is worse, mild cognitive impairment and dementia more prevalent, and vascular risk factor burden increased in underserved black and Hispanic populations.[37] Possibly such movements might result in less economic and social deprivation, and better education all leading to improved health and wellbeing.

5. Challenges in promoting and maintaining brain health

Mental health and social wellbeing research and initiatives seldom link with efforts to fight ailing brains (Box 1). An abyss remains between those who focus on the body and the brain and those who study and act on the results of the brain's activities. Besides, healthy lifestyles in most of the world are besieged by urbanization, mechanization, disparities in costs of living and

earnings in many LMICs, and politicization stemming from populist movements (science is being suppressed for political and financial gain). As people need to work more to maintain their standard of living, their physical and mental health is often sacrificed. This occurs often among those of lower socioeconomic status, the group that has been the hardest hit by the lockdowns associated with the pandemic. While increasingly problematic in rich countries, the problem is even more severe in poorer ones. Almost 71% of the increase in the global prevalence and burden of dementia by 2050 will take place in LMICs,[28] where risk of dementia is not declining.[38]

According to the WHO *Atlas: Country Resources for Neurological Disorders*, only one fourth of countries globally have neurological health policies and they are virtually absent in the majority of LMICs.[39] Thus, most of our knowledge on the association of risk factors with dementia is based on data from high-income countries.[40] Our understanding about the wide array of ways in which socioeconomic conditions could affect dementia is limited. Work environments, human capital, social and cultural capital are all related to socioeconomic background. More research is needed on the role of these factors in developing countries, particularly LMICs.[14,41]

6. In search of an overarching definition

The WHO definition of health is comprehensive, concise, and has existed for seven decades. We need an agreed overarching definition of brain health, and objective methods to quantify it (Box 2).[11,42–48] The current definitions focus on absence of disease, and omit mental health,

quality of life, and happiness. They can all be united through an understanding of the brain. The management (including prevention) of non-communicable diseases needs to follow a life-course approach. Convergent efforts to promote brain health may take us closer to the WHO definition of health. Earlier, we defined brain health as "*a state of complete physical, mental, and social wellbeing through a full, balanced, continuous development and exercise of the brain.*"[42] According to this definition, brain health is the key to overall health and wellbeing.[42] Our definition of brain health, as the 'candle', forms the basis for the WHO definition of mental health[46] (Box 2), which would provide us with a key to interpretation and action plans. The most promising strategy of protecting and promoting brain health is a lifetime holistic approach to prevention, accepting that prevention begins even before conception through transgenerational, biological, and social effects; (Figure 2).

Mental and physical health are interactive, and brain health is the platform through which both can happen. The plasticity of the brain is enormous and brain development can occur lifelong by nurturing and exercising the brain cognitively, psychologically, and socially and providing sufficient and undisturbed sleep. Physical and cognitive exercise and sleep (which also promotes learning and neuroplasticity) are particularly important with increasing age. Brain health is essential for physical and mental health as well as social wellbeing, productivity, and creativity.

7. Conclusions

Traditionally, cardiovascular disorders, which included stroke, were the public health priority because of their leading role as the cause of death and disability. Currently, brain disorders have become the leading cause of death and disability combined (18% of all-cause DALYs). We suggest considering brain health as the top priority. Second, in line with the ICD-11 in which stroke has moved from cardiovascular disorders to the disorders of the nervous system, we suggest for the Global Burden of Disease Study to include stroke in the group cause of neurological disorders. Third, the COVID-19 pandemic has brought tragedy and transformation; It has intensified the need for physical, psychological, environmental, and social wellbeing; while physical isolation has increased the connectivity capacity for distant and cooperative interactions that could prove to be new avenues in fostering brain health. Therefore, we should take a ‘candle’ and go in ‘together’ to examine ‘the elephant in the dark’ to minimize our differences. All need to work synergistically to enhance brain health for increased overall health, productivity, and wellbeing.

Box 1: Obstacles to protecting and promoting brain health

- Population growth and population ageing are non-modifiable factors fostering brain degeneration and brain health deterioration.
- Minimal collaboration between the public, sociologists, political scientists, economists, neurologists, psychiatrists, psychologists, basic researchers, medical communicators, and policymakers on fighting diseased brains and to maintain and promote brain health.
- Limited understanding of the basic science mechanisms contributing to optimal brain health and prevention of decline.
- Varying health needs and gaps in different regions and countries as to socioeconomic status demand different policymaking and prioritization of resources.
- Unhealthy lifestyles, and mental and physical health sacrifices ascribable to urbanization, mechanized life, unbalanced costs of living, and inequity.
- Climate instability, threatening health and life itself.
- Political instability, fostering wars and conflicts around the world.
- Inadequate understanding, especially in low and middle-income countries, that brain health is affected by the majority of diseases including communicable, non-communicable, nutritional, and life-style diseases.
- Scarcity and diversity of available knowledge and lack of concordance between scientists and clinicians dealing with dementia patients and mental disorders, in particular.

- Limited resources for neurological disorders, gaps in scientific evidence, inconsistent health policies, and poor healthcare access and preventive health implementation strategies in all countries, particularly in middle-income ones.
- The widespread dualistic and reductionist 'mind-body' paradigms need to be challenged and overcome with integrative paradigms.
- Lockdowns during the pandemic makes it difficult to maintain standards of living, particularly among those of a low or middle socioeconomic status.
- The COVID-19 pandemic has crowded out attention to and resources for other health issues, including brain health.

Box 2: Definitions of brain health

- By the American Heart Association/American Stroke Association: "*average performance levels among all people at that age who are free of known brain or other organ system disease in terms of decline from previously documented levels of function or as adequacy to perform all activities that the individual wishes to undertake*."[11] The definition was recently updated to: "*Pragmatically, it is the preservation of neuronal function to meet the demands of everyday life, operationally defined in terms of the capacity to function adaptively in one's environment …. The ability to think, solve problems, remember, perceive, and communicate is crucial to successful living; their loss can lead to helplessness and dependency*."[12]
- By the World Federation of Neurology:[6] "*Brain health is a critical piece of your overall health. It underlies your ability to communicate, make decisions, problem-solve and live*

a productive and useful life. Because the brain controls so much of daily function, it is arguably the single most valuable organ in the human body."

- By Center for Brain Health (the University of Texas at Dallas):[44] "*a person's ability to function well in daily life and work. This includes making wise decisions, solving problems, interacting successfully with others, and enjoying an emotional balance. All of these functions demand the capacity to remember, comprehend and learn; to process information, events and people; to think strategically; and to be innovative in solving problems as they arise*."
- By the US Centers for Disease Control and Prevention:[45] "*an ability to perform all the mental processes that are collectively known as cognition, including the ability to learn new things, intuition, judgment, language, and remembering*."
- By the World Health Organization: "*Mental health is a state of well-being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community*"[46] and "*The prevention of neurological disorders rests upon the promotion and development optimal brain health across the life course. Good brain health is a state in which every individual can learn, realize their potential, and optimize their cognitive, psychological, neurophysiological, and behavioral responses while adapting to changing environments*."[48]
- By Galderisi et al:[47] "*Mental health is a dynamic state of internal equilibrium which enables individuals to use their abilities in harmony with universal values of society. Basic cognitive and social skills; ability to recognize, express and modulate one's own*

emotions, as well as empathize with others; flexibility and ability to cope with adverse life events and function in social roles; and harmonious relationship between body and mind represent important components of mental health which contribute, to varying degrees, to the state of internal equilibrium."

- By Wang et al:[43] "*preservation of optimal brain integrity and mental and cognitive function at a given age in the absence of overt brain diseases that affect normal brain function*."
- By Hachinski et al:[42] "*a state of complete physical, mental, and social wellbeing through a full, balanced, continuous development and exercise of the brain*."

Box 3: Next steps in fostering brain health

- Make brain health the top priority worldwide.
- Gathering and converging interdisciplinary expertise on brain health.
- Recognizing the importance of humanities, the arts, and spirituality for wellbeing.
- Developing global workgroups and workforces aiming to promote healthy aging through the life-course, in particular from childhood, and to eliminate health disparities.
- Establishing an ecosystem to synergistically engage the populace, patients, health-care providers, payers for health services, and policymakers.
- Involve the electronic, social, and print media, as well as communication artists to foster communication among all stakeholders in the language they understand best and using their preferred channels.
- Improve all pillars of the brain quadrangle (Figure 3).

- Promoting vigorous discussions to facilitate synergistic action plans by researchers, organizations, governments, non-government organizations, and pharmaceutical companies to invest in top priorities and new ideas.
- Gaining systematic knowledge, being open to new ideas and hypotheses, and being critical to all the ideas and concepts.
- Consolidating current knowledge and addressing knowledge gaps in brain function, brain diseases, and associated risk factors.
- Developing novel point of care devices and precision medicine and omics solutions to improve diagnosis, holistic risk prediction, and prognostication.
- Using data science and artificial intelligence tools combined with trans-omics to identify novel molecular targets and novel therapeutics to improve outcomes for brain health
- Being visionary and using initiative to generate hypotheses and assess their underlying evidence and how to test them.
- Consider the underlying definitions and approaches when examining risks and protective factors of dementia.
- Building provisional criteria and metrics to develop a common vocabulary and data-based criteria in assessment of the healthy and diseased brain to allow systematic comparisons and meta-analyses, and to develop metrics to assess and quantify brain health.
- Integrating prevention of stroke, heart disease, and dementia with commitments from the endorsing organizations for implementing the joint prevention of stroke, heart disease, and dementia and promotion of brain health.

- Highlighting the expanding burden of neurological disease to convince policymakers to allocate resources on preventive measures against ischemic heart disease, stroke, and dementia and on promoting protective factors at the population level.
- Facilitating infrastructures to boost productivity with a higher degree of cognitive competence to result in more productive jobs with more satisfactory quality of life.
- Strengthening local health systems, improving surveillance to generate high-quality data, and aiding caregivers and patients to access cost-effective preventive health strategies to reduce the burden of brain diseases, particularly in developing countries.
- Making care affordable and accessible, preferably through Universal Health Coverage and fostering effective delivery of primary health care.
- Promoting primary prevention of modifiable risk factors through both high-risk (i.e., targeting population at a higher risk of developing a disease) and mass (population-based) approaches.
- Tailoring cost-effective, realistic, and actionable recommendations and priorities to age, gender, ethnocultural, and socioeconomic status of target populations.
- A marked growth in repurposed agents has been observed in the pipeline with progressive emphasis on non-amyloid targets,[49] which should be promoted.
- Improving general awareness about rare neurological diseases, comprising over half of all rare diseases,[50] especially because early treatments are now available for many disorders and able to improve the quality of life of patients and caregivers.

- Realizing that brain health maintenance and promotion are lifelong; positive and negative brain health behaviors form in childhood and fostering positive behaviors may optimize maternal and infant health.

Legends

***Figure 1*. The Blind Men and the Elephant**

"Each in his own opinion
Exceeding stiff and strong,
Though each was partly in the right,
And all were in the wrong!"
(Poem by John Godfrey Saxe)

Source of picture: Himmelfarb et al. *Kidney Int* 2002; 62(5): P1526 (artist: G. Renee Guzlas). All rights reserved ©. Reproduced by permission.
Source of Story: Rumi J al-Din. The elephant in the dark. In: The Masnavi, Book Three (Oxford World's Classics), 1st edn. Oxford: Oxford University Press, 2014: 78–83.

***Figure 2:* Approach to protecting and promoting brain health**

Protecting and promoting optimal brain health occurs across the life-course, from fetal development through death. It requires a whole-of-government and whole-of-society approach, given its many interacting social, economic, ecological, and political as well as biomedical and psychological determinants. It also requires a whole-of-global-governance approach, given extensive global movement of people, capital, goods and services, as well as myriad other factors that can be beneficial for (e.g., knowledge about new medical treatments) or deleterious to (e.g., environmental contaminants) optimal brain health. Thus, optimizing brain health truly requires the synergistic

efforts of heads of state and government, health care systems, public health systems, the scientific communities, and many other non-government organizations from the most powerful countries in the world, when they meet together annually to govern health and its many determinants.

Figure 3. **Brain quadrangle**

(i) establishing a framework for regular surveillance (monitoring and evaluation of risk factors) and health services at local, national, and international levels via community-based surveys and electronic health records;

(ii) implementation of integrated population-wide strategies to reduce modifiable risk factors, such as hypertension and diabetes mellitus, with a range of approaches such as task-sharing and mobile technology across the lifespan; (This will reduce prevalence and incidence of brain diseases);

(iii) effective planning of acute care services, workforce training, and capacity building, with monitoring of quality indicators nationally and internationally; (This will reduce mortality of brain diseases); and

(iv) promoting access to interdisciplinary care, training for caregivers, and capacity building of community health workers and other health care providers for stroke rehabilitation to improve quality of life and prolong health.

Contributors

VH conceptualized this Perspective. AA performed the search and curated the data, comments, and edits. AA and VH wrote the original draft. All authors revised and edited the manuscript and approved the final version. VH had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Role of the funding source

None

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Figure 1

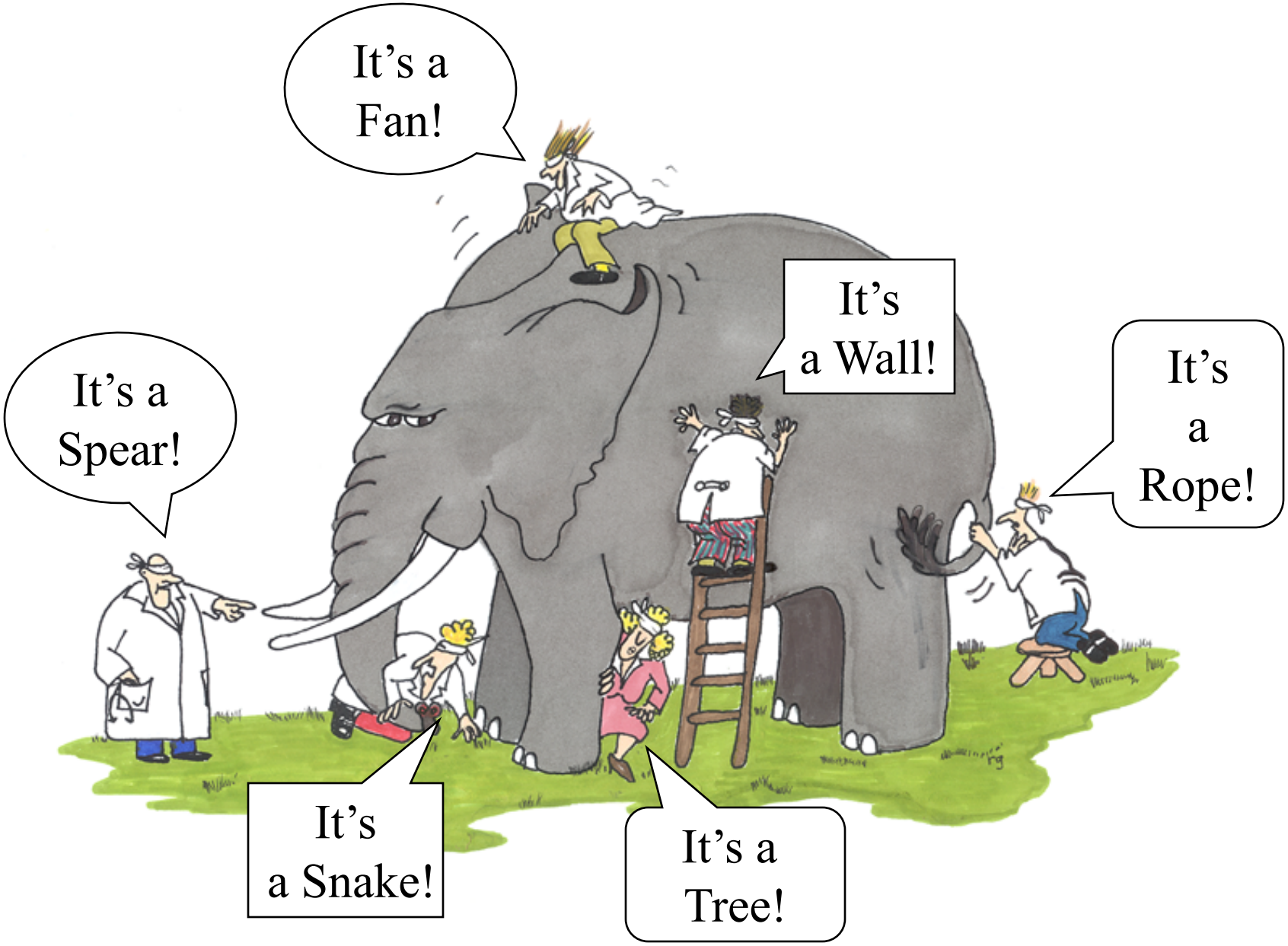


Figure 2

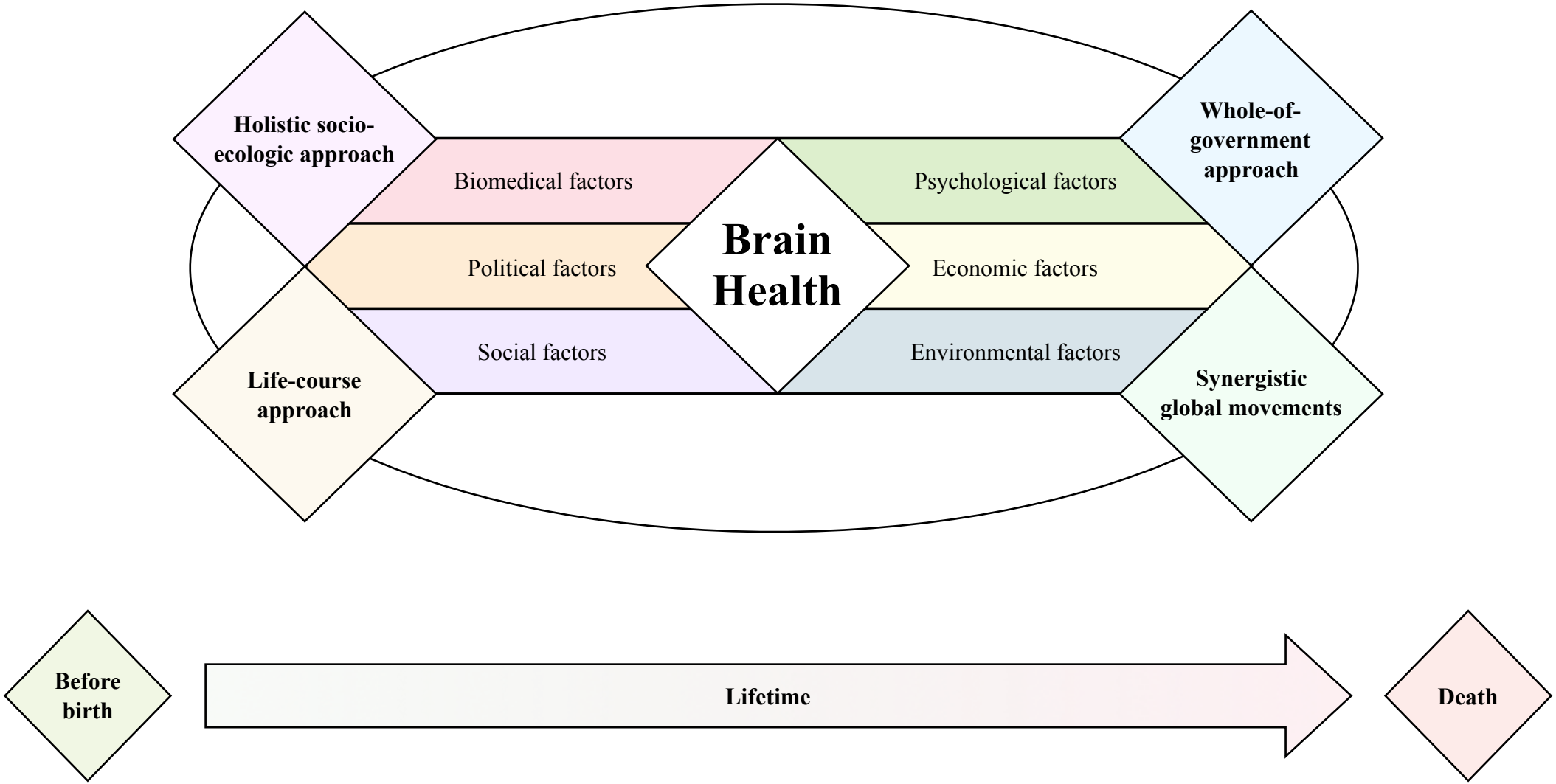
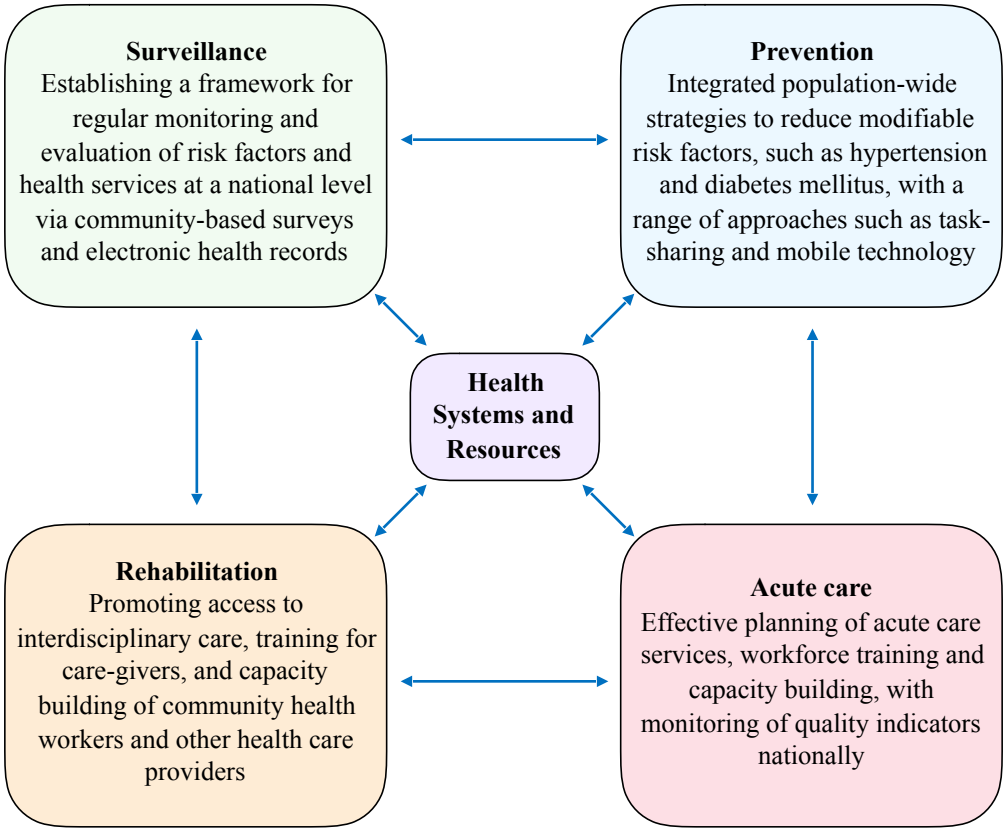

Holistic socio-ecologic approach
Whole-of-government approach
Biomedical factors
Psychological factors
Political factors
Brain Health
Economic factors
Social factors
Environmental factors
Life-course approach
Synergistic global movements
Before birth
Lifetime
Death

Figure 3


Surveillance
Establishing a framework for regular monitoring and evaluation of risk factors and health services at a national level via community-based surveys and electronic health records
Prevention
Integrated population-wide strategies to reduce modifiable risk factors, such as hypertension and diabetes mellitus, with a range of approaches such as task-sharing and mobile technology
Health Systems and Resources
Rehabilitation
Promoting access to interdisciplinary care, training for care-givers, and capacity building of community health workers and other health care providers
Acute care
Effective planning of acute care services, workforce training and capacity building, with monitoring of quality indicators nationally

Highlights

- Brain health should be recognized as the top global priority of health policies
- Brain health can be developed, improved, and maintained as we age
- Human health is interconnected with all life forms and environments
- There is a lack of a uniform definition of brain health endorsed by major societies
- Protecting and promoting brain health demands a lifetime holistic approach.